Induced pluripotent stem cells show metabolomic differences to embryonic stem cells in polyunsaturated phosphatidylcholines and primary metabolism.

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Public Summary:
Induced pluripotent stem cells are different from embryonic stem cells as shown by epigenetic and genomics analyses. Depending on cell types and culture conditions, such genetic alterations can lead to different metabolic phenotypes which may impact replication rates, membrane properties and cell differentiation. We here applied a comprehensive metabolomics strategy incorporating nanoelectrospray ion trap mass spectrometry (MS), gas chromatography-time of flight MS, and hydrophilic interaction- and reversed phase-liquid chromatography-quadrupole time-of-flight MS to examine the metabolome of induced pluripotent stem cells (iPSCs) compared to parental fibroblasts as well as to reference embryonic stem cells (ESCs). With over 250 identified metabolites and a range of structurally unknown compounds, quantitative and statistical metabolome data were mapped onto a metabolite networks describing the metabolic state of iPSCs relative to other cell types. Overall iPSCs exhibited a striking shift metabolically away from parental fibroblasts and toward ESCs, suggestive of near complete metabolic reprogramming. Differences between pluripotent cell types were not observed in carbohydrate or hydroxyl acid metabolism, pentose phosphate pathway metabolites, or free fatty acids. However, significant differences between iPSCs and ESCs were evident in phosphatidylcholine and phosphatidylethanolamine lipid structures, essential and non-essential amino acids, and metabolites involved in polyamine biosynthesis. Together our findings demonstrate that during cellular reprogramming, the metabolome of fibroblasts is also reprogrammed to take on an ESC-like profile, but there are select unique differences apparent in iPSCs. The identified metabolomics signatures of iPSCs and ESCs may have important implications for functional regulation of maintenance and induction of pluripotency.

Scientific Abstract:
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